RESPIRATORY MEDICINE (1997) **91**, 443–448


## Original Articles

# Reduced forced expiratory flow in schoolchildren with respiratory symptoms: The Odense Schoolchild Study

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In the present population-based study, spirometric lung function was assessed in symptomatic schoolchildren with and without asthma as compared to an asymptomatic reference group. The primary aim was to investigate if impaired lung function could be demonstrated in symptomatic schoolchildren, even in the absence of diagnosed asthma.

Spirometry [forced vital capacity (FVC), forced expiratory volume in 1 s ($FEV_1$), 50% of forced expiratory flow (FEF 50%) and 75% of forced expiratory flow (FEF 75%)] and anthropometric measures (standing height, weight, skin fold thickness, and length and circumference of the upper arm) were obtained from 1369 8–10-year-old children (81·5% of the eligible population) during the school year 1985–86. In 1321 of those subjects (96·5% of those examined), a self-administered questionnaire was completed. Thirty-five children belonging to ethnic minorities were excluded, thus 1286 subjects were included for further analysis. Point prevalences concerning asthma and respiratory symptoms (wheeze, cough and shortness of breath) were obtained.

Thirty-seven children reported asthma and one or more asthma-like symptoms (symptomatic asthmatics), whereas 40 children denied having asthma, although claiming one or more asthma-like symptoms (symptomatic non-asthmatics). In both symptomatic groups, FEF 50% and FEF 75% were reduced relative to the reference group, the deficit being larger in the symptomatic asthmatics. FEF 75% was found to be more reduced than FEF 50%. $FEV_1$ and FVC did not differ significantly between groups.

It is concluded that only half of the schoolchildren with respiratory symptoms usually associated with the presence of asthma actually reported having this disease. These results demonstrate the presence of reduced lung function in symptomatic, reportedly non-asthmatic, children, suggesting clinically important underdiagnosis of asthma. More severe impairment of lung function was found in known asthmatics, also implying some degree of undertreatment.

RESPIR. MED. (1997) **91**, 443–448

## Introduction

The mortality and morbidity of asthma are increasing worldwide (1–3). Asthma, not treated properly, may cause progressive loss of lung function (4–6). Thus, early identification of asthmatics is of prognostic importance. This study was aimed at the identification of subjects with asthma-like symptoms having signs of impaired lung function with or without reported asthma, among children aged 8–10 years.

## Population

The Odense Schoolchild Study is a longitudinal study describing the development of lung function in health and disease in a population of schoolchildren whom, in 1985, were enrolled in the third grade in the public schools in Odense, Denmark. The overall study design has been described in detail previously (7).

Received 20 December 1995 and accepted in revised form 25 September 1996.
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0954-6111/97/080443+06 $12.00/0

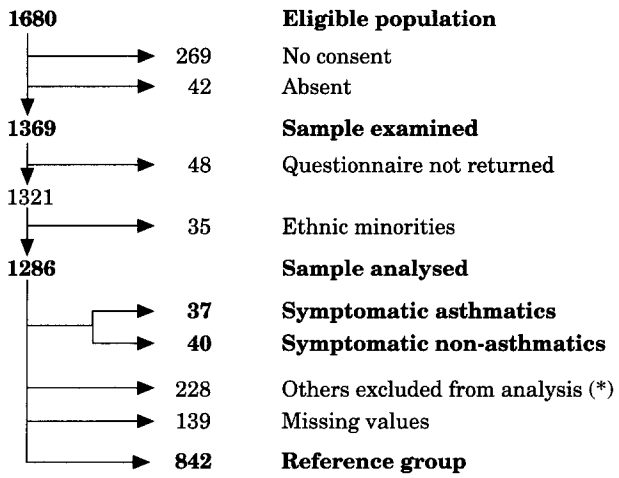


FIG. 1. Population, losses and samples. *Others excluded are those subjects who answered: (a) 'Yes' to Q1 and 'No' or 'Do not know' to Q2–6; (b) 'Yes' to Q7–10; and (c) 'Do not know' to Q1–10.

Briefly, in 1985, there were 1680 children aged 8–10 years in the third grade in 36 public schools participating in the investigation. These children were all invited to join the survey, and 1411 children (84·0%) obtained their parents' or guardians' written consent to participate. Two hundred and sixty-nine children did not obtain consent, and 42 were absent from school at the time of survey at their school. Of these 1369 children, 48 did not return the questionnaire. As the relationship between body size and lung function is known to be different in various ethnic groups (8,9), only Caucasian children whose parents were both born in Northern Europe were included in the analysis, so 35 subjects belonging to ethnic minorities were omitted from further analysis. The analysed sample thus included 1286 children, 647 boys and 639 girls, constituting 76·5% of the total eligible population (Fig. 1).

The study was recommended by the municipal School Board and approved by the local Ethical Committee and the Danish Data Surveillance Authority.

## Methods

### EXAMINATION

Each child received a questionnaire concerning respiratory symptoms, medical history, drug intake and smoking habits. The questionnaire was completed at home with the aid of the child's parents or guardians. The questions used in the present analysis are listed in Table 1.

The children were investigated in a mobile office (a modified caravan) at their school. The office was fully equipped for the survey, and heating (in the winter) and ventilation (in the summer) kept the temperature between 10 and 24°C [median 21·0, interquartile range (IQR) 2·0]. The examination period was between 0800 and 1400h on each school day from October to June 1986.

Standing height to the nearest centimetre and weight to the nearest kilogram were measured with light indoor clothes and shoes on. The length and the circumference of the upper arm was measured to the nearest centimetre. Skin-fold thickness over the triceps muscle and over the inferior scapular angle were measured with a Harpenden skinfold calliper as indices of body fat deposition. The degree of sexual maturation was rated on a scale from 1 to 5 (10). The children were classified according to their ethnic relations. Spirometry was performed using a McDermott dry bellows spirometer (Garw Electronic

TABLE 1. Questions on asthma or respiratory symptoms in the questionnaire (translated from Danish)

| | |
|---|---|
| Q1 | Do you have asthma, i.e. periods of wheeze and/or cough? |
| Q2 | Do you have wheeze and/or cough at rest? |
| Q3 | Do you have wheeze and/or cough when you are exercising? |
| Q4 | Do you have wheeze and/or cough in foggy weather? |
| Q5 | Do you feel shortness of breath at night? |
| Q6 | Do you feel shortness of breath in the morning? |
| Q7 | Do you have hay fever, i.e. allergic nose/eye catarrh (grass, animals, dust)? |
| Q8 | Do you have bronchitis, i.e. periodic cough during several days/weeks? |
| Q9 | Are you receiving treatment for any medical condition? |
| Q10 | Do you smoke? |

Q1–8 could be answered 'Yes', 'No', or 'Do not know'. Q9 and 10 could be answered 'Yes' or 'No'.

Instruments, Penarth, Wales, U.K.) connected to a matrix printer, permitting inspection of the flow–volume curve immediately after the manoeuvre. Each subject performed at least three accepted forced vital capacity (FVC) manoeuvres in the standing position in accordance with the European standarized recommendations (11). Nose-clips were applied. The spirometer was calibrated each morning using a 1-l calibration syringe. The variation was within ± 2% of the mean.

### ANALYSES

According to the answers given in the questionnaire, the children could be allocated to one of three groups: (a) those who had an affirmative answer to Q1 ('do you have asthma?') and to one or more of Q2–6, i.e. symptoms related to asthma (symptomatic asthmatics); (b) those who had given a negative answer to Q1 but affirmative answers to one or more of Q2–6 (symptomatic non-asthmatics); and (c) those who had given negative answers to Q1–10 (reference group) (Fig. 1). In the reference group, the association between lung function and the anthropometric measurements were analysed using stepwise multiple linear regression analysis, with the spirometric measurements as the dependent variables and the anthropometric measurements as the independent variables, resulting in prediction equations for lung function indices in the study population.

Using these prediction equations, each child's lung function values were expressed as a percentage of the predicted value. The reference group included no subjects with missing values (Fig. 1), and in the two symptomatic groups, only subjects with affirmative answers to the relevant questions were included. Children with rhinitis might have reduced lung function (12,13), and therefore they were excluded from the reference group, as were children reporting bronchitis, smoking or medical treatment.

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) (14). Stepwise multiple regression analyses were performed using a significance level of 0·05 for entry and 0·10 for exclusion from the model. Mean values were compared with Student's two-tailed *t*-test. Differences were considered significant if $P$ was 0·05 or less. A 95% confidence interval for the mean (CI) was calculated using the program 'Confidence Interval Analysis' (15).

## Results

In this study, 77 of 1286 children (6·0%) gave affirmative answers to one or more questions about respiratory symptoms. Only 48·1% of these 77 symptomatic children also stated that they had asthma. The most common single symptom was wheeze and/or cough when exercising (65%), followed by wheeze and/or cough in foggy weather (56%) and shortness of breath at night (29%).

In Table 2, the mean value and the 95% CI of the anthropometric measurements are shown for each group and gender separately. Significant differences in the anthropometric measurements between the reference group and the symptomatic groups were seen, indicating need for correction for these variables when comparing the lung function values between the groups. The percent predicted FVC and forced expiratory volume in 1 s ($FEV_1$), as shown in Table 3, were not statistically significantly reduced in any of the symptomatic groups as compared to the reference group. In the symptomatic asthmatics, 50% of forced expiratory flow (FEF 50%) was 16% lower than in the reference group, and FEF 75% was 25% lower, whereas in the symptomatic non-asthmatics, FEF 50% was significantly reduced by 7% and the FEF 75% by 8%.

There were no missing values in the anthropometric and spirometric data. Of 1369 children, 1321 returned the questionnaire. Two hundred and forty-three subjects had missing values in Q1–10. In 80% of these subjects, the missing values were in Q2–4. No statistically significant differences were found comparing the spirometric or anthropometric measurements from subjects returning a fully completed questionnaire with subjects not returning the questionnaire, or having missing answers to any relevant questions.

## Discussion

In the present study, 77 schoolchildren out of a random sample of 1286 children 8–10 years of age in a questionnaire gave affirmative answers to one or more questions about respiratory symptoms. About half of these symptomatic children also reported that they had asthma.

The boy/girl ratio of the symptom prevalence was 1·2 (42/35), whereas it was 1·5 (22/15) for asthma, indicating that girls at this age have their symptoms diagnosed as asthma less frequently than boys. Comparable gender differences in symptom prevalence has been reported previously (6,16,17). This paper focuses on subjects complaining of respiratory symptoms with or without the diagnosis of asthma. The questionnaire asked about the actual presence of symptoms (Do you have . . .?) The reported frequency of respiratory symptoms is, therefore, a point

TABLE 2. Mean values, 95% confidence intervals of the mean and significance levels for the anthropometric measurements in the three groups of subjects used in the analysis

| | | Reference group ♂: $n$=414 ♀: $n$=428 | | Symptomatic asthmatics ♂: $n$=22 ♀: $n$=15 | | | Symptomatic non-asthmatics ♂: $n$=20 ♀: $n$=20 | | |
|---|---|---|---|---|---|---|---|---|---|
| Parameter | Gender | Mean | 95% CI | Mean | 95% CI | $P$ | Mean | 95% CI | $P$ |
| Height (cm) | ♂ | 141·5 | 141·0–142·2 | 140·7 | 138·4–143·0 | | 139·7 | 137·1–142·2 | |
| | ♀ | 140·7 | 140·1–141·3 | 137·7 | 135·0–140·5 | | 137·6 | 134·8–140·3 | * |
| Weight (kg) | ♂ | 34·0 | 33·5–34·6 | 32·0 | 30·5–33·5 | * | 34·8 | 31·7–37·9 | |
| | ♀ | 33·4 | 32·9–34·0 | 31·7 | 29·2–34·1 | | 32·4 | 30·1–34·6 | |
| Circumference arm (cm) | ♂ | 20·8 | 20·6–21·0 | 20·0 | 19·4–20·5 | * | 21·4 | 20·0–22·8 | |
| | ♀ | 21·3 | 21·0–21·5 | 21·1 | 20·4–21·9 | | 21·6 | 20·7–22·4 | |
| Subscapular skinfold (mm $10^{-1}$) | ♂ | 75·6 | 71·7–79·6 | 58·5 | 51·1–65·8 | † | 93·9 | 57·4–130·3 | |
| | ♀ | 90·1 | 85·6–94·7 | 83·1 | 70·0–96·3 | | 88·2 | 73·8–102·6 | |
| Pubertal stage (1–5) | ♂ | 1·03 | | 1·00 | | | 1·00 | | |
| | ♀ | 1·55 | | 1·20 | | | 1·65 | | |
| Age (years) | ♂ | 9·71 | 9·67–9·75 | 9·66 | 9·52–9·79 | | 9·62 | 9·41–9·83 | |
| | ♀ | 9·66 | 9·62–9·70 | 9·61 | 9·39–9·83 | | 9·65 | 9·40–9·90 | |

♂, boys; ♀, girls. Values significantly differing from the mean in the reference group are indicated: *$P$<0·05; †$P$<0·005; 95% CI, 95% confidence interval of the mean.

prevalence, and must not be regarded as, for example, a 1-yr prevalence. The point prevalence found in this study are similar to point prevalences reported in several other European studies (3,8,12,18), but less than the 1-yr prevalences found in North America and Australia (2,19). These differences in prevalence between different parts of the world may be caused by the two methods of expressing prevalence (point *vs* 1-yr), but an impact of differences in lifestyle and environmental factors cannot be excluded and is supported by the findings of an international study (20). Standardized multinational surveys on asthma epidemiology are proceeding (21).

As lung function is highly correlated to anthropometric measurements, especially height, a comparative analysis of lung function must include an analysis of differences in anthropometry, as shown in Table 2. There are significant differences in several anthropometric measurements, especially between the reference group and the symptomatic boys, indicating an influence of the presence of asthma on somatic growth. In order to compensate for these differences

TABLE 3. Mean values, 95% confidence intervals of the mean and significance levels for the percent predicted lung function indices in the three groups of subjects used in the analysis

| | Reference group ($n$=842) | | Symptomatic asthmatics ($n$=37) | | | Symptomatic non-asthmatics ($n$=40) | | |
|---|---|---|---|---|---|---|---|---|
| Parameter | Mean | 95% CI | Mean | 95% CI | $P$ | Mean | 95% CI | $P$ |
| FVC (% predicted) | 100·0 | 99·3–100·7 | 100·8 | 96·3 ± 105·3 | | 101·1 | 98·2–104·0 | |
| $FEV_1$ (% predicted) | 100·0 | 99·3–100·7 | 94·8 | 88·9–100·8 | | 99·8 | 96·8–102·9 | |
| FEF 50% (% predicted) | 100·0 | 98·8–101·2 | 84·0 | 75·8–92·2 | † | 92·7 | 87·9–97·6 | * |
| FEF 75% (% predicted) | 100·0 | 98·4–101·6 | 75·2 | 66·8–83·6 | † | 91·9 | 85·1–98·6 | * |

Values significantly differing from the mean in the reference group are indicated: *$P$<0·05; †$P$<0·005; 95% CI, 95% confidence interval of the mean.

in body size between the groups, an internal reference group was defined comprising only those subjects explicitly denying asthma and any respiratory symptoms. Thus, the comparative analysis of lung function (Table 3) was based on results expressed as percent predicted with reference to this internal reference group. As a correction for body size has been made and the lung function values are expressed on an arbitrary scale, boys and girls can be analysed together.

These data showed that FVC and $FEV_1$ were not significantly affected by the presence of respiratory symptoms in schoolchildren aged 8–10 years. In children complaining of respiratory symptoms, FEF 50% and FEF 75% were significantly lower than in the reference group; FEF 75% was more reduced than FEF 50%. Reporting respiratory symptoms together with asthma was associated with a greater deficit in level of lung function than the reporting of symptoms without asthma.

This is in accordance with the findings of Gold *et al.* who, in a study of 10 792 schoolchildren, demonstrated that the FEF 25–75% in children with 'asthma ever' and current wheeze was reduced to a larger extent than in children with current wheeze but no diagnosis of asthma (22). They also found $FEV_1$ to be significantly reduced in children with current wheeze, regardless of the diagnosis of asthma, as compared to a reference group, the reduction being of the same magnitude as found in the present investigation. The lack of significance in the present study might, therefore, be explained by the smaller number of subjects examined.

This analysis shows the forced expiratory flows to be more sensitive parameters than the traditionally used $FEV_1$. The flow at low lung volume is more reduced than the flow when half of the FVC has been exhaled, reflecting that the pathophysiological changes occur predominantly in the small airways (23).

The forced expiratory flows being reduced in the symptomatic children without asthma as compared to the reference group might suggest some degree of asthma underdiagnosis. The average reduction, however, is not nearly as large as that found in the symptomatic subjects with a positive diagnosis of asthma. This larger deficit in lung function among children with known asthma might indicate some undertreatment of the disease, as one would expect at least part of the diagnosed subjects to be on medical treatment tending to normalize lung function, whereas the symptomatic subjects without the diagnosis of asthma will probably receive no treatment.

Several studies in children have demonstrated prevalences of asthma-like respiratory symptoms exceeding that of diagnosed asthma (24–28). The present authors have recently shown that 26% of such symptomatic children, not previously diagnosed with asthma, had bronchial hyper-responsiveness either as an increased peak flow variability or as an increased dose–response slope in a methacholine provocation test (29), strongly suggesting that these children were actually asthmatic.

However, respiratory symptoms may not always be associated with asthma, as indicated by Lee *et al.* (30) who in 1981 showed that one-third of children with recurrent wheeze failed to react to a histamine challenge test. Similarly, Backer and Ulrik showed that in children with just one respiratory symptom, only 14 and 19% had bronchial hyper-responsiveness to histamine or exercise, respectively (31). Thus, the magnitude of underdiagnosis is probably not as large as the frequency of symptoms indicate.

In this study, about 18% of the questionnaires had missing values in one or more questions. Eighty percent of the missing values were in three of the questions about respiratory symptoms, a phenomenon that can probably be explained by the schematic layout of this part of the questionnaire. There were no significant differences in the spirometric or the anthropometric measurements between subjects with one or more missing values in the relevant questions and those without. On the basis of these analyses, the authors believe that neither non-responders nor missing values seriously biased the results of this investigation.

It is concluded that 6% of Danish schoolchildren aged 8–10 years complained of respiratory symptoms compatible with the presence of asthma, but only half of them reported asthma. FEF 50% and FEF 75% were significantly reduced in symptomatic children, among whom those with asthma showed the largest deficit in lung function. These results suggest some underdiagnosis as well as undertreatment of asthma in the population.

## Acknowledgements

Jesper Boldsen, Department of Social Health, Odense University gave valuable statistical advice.

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